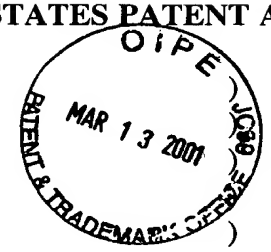
Patent
Attorney's Docket No. 028723-060

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



#31
Plunkett
3/20/01

In re Patent Application of

GRAY et al

Application No.: 08/477,316

Filed: June 7, 1995

For: CHROMOSOME-SPECIFIC STAINING TO DETECT GENETIC REARRANGEMENTS ASSOCIATED WITH CHROMOSOME 3 AND/OR CHROMOSOME 17

Group Art Unit: 1631

Examiner: A. Marschel

BRIEF FOR APPELLANT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

This appeal is from the decision of the Primary Examiner dated August 15, 2000 (Paper No. 26), finally rejecting claims 1, 48 and 50-58, which are reproduced as an Appendix to this brief.

A check covering the [ ] $155.00 (220) [X] $310.00 (120) Government fee and two extra copies of this brief are being filed herewith.

The Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17, and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800. This paper is submitted in triplicate.

I. Real Party in Interest

The present application is assigned to The Regents of the University of California.

II. Related Appeals and Interferences

Neither the assignee nor their legal representative know of any other appeal or interferences which will affect or be directly affected by or have bearing on the Board's decision in the pending appeal.

III. Status of Claims

The Application was filed on June 7, 1995 with 1 independent claim (claim 1). On September 4, 1996, an Official Action was mailed (Paper No. 5) rejecting the claim.

On March 4, 1997, claim 1 was amended. On June 9, 1997, an Official Action was mailed finally rejecting claim 1. Claim 1 was amended and new claims 48-50 were added on December 9, 1997. These amendments were denied entry by the Examiner in the Advisory Action (Paper No. 12) mailed January 8, 1998, on the grounds that the new claims raised new issues, because they were not deemed to place the application in better form for appeal, and because they presented additional claims without canceling a corresponding number of finally rejected claims. Applicants petitioned the December 9, 1997 entry under 37 C.F.R. § 1.129(a). An Official Action was mailed on June 30, 1998 rejecting claims 1 and 48-50. Applicants filed an amendment on December 30, 1998 deleting claim 49, amending claims 1, 48, and 50 and adding new claims 51-58. On March 17, 1999, an Official Action (Paper No. 18) was mailed finally rejecting claims 1, 48, and 50-58. The Applicants filed a reply on August 17, 1999. An Official Action was mailed on November 29, 1999 withdrawing the finality in response to Applicants' Reply and newly rejecting claims 1, 48, and 50-58. Claims 1, 48, and 50 were amended on May 25, 2000. In an Official Action (Paper No. 26) mailed on August 15, 2000, claims 1, 48, and 50-58 were finally rejected.

On December 14, 2000, appellant appealed from the final rejection of claims 1, 48, and 50-58.

The status of the claims as set out in Paper No. 26 was and is as follows:

allowed claims: none

claims objected to: none

claims rejected: 1, 48, and 50-58

IV. Status of Amendments

All amendments have been entered.

V. Summary of the Invention

Applicant's invention is directed toward a method of staining targeted chromosomal material based upon a nucleic acid segment employing unique sequence high complexity nucleic acid probes of greater than 50,000 bases, wherein said targeted chromosomal material is a genetic rearrangement associated with chromosome 3 and/or chromosome 17 in humans.

VI. The Issues

1. The Examiner has rejected claims 1, 48, and 50-58 under 35 U.S.C. § 103(a) as purportedly obvious over U.S. Patent 4,710,465 to Weissman et al. in view of Lichter et al. (1988)[1] and Le Beau et al. (1985)[2] and Drabkin et al. (1985)[3]. These are appended hereto as Appendix B.

2 The Examiner has provisionally rejected claims 1, 48, and 50-58 under the

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[1]Lichter, P., Cremer, T., Tang, C., Watkins, P.C., Manuelidis, L., and Ward, D.C. (1988) Rapid detection of human chromosome 21 aberrations by *in situ* hybridization. *PNAS USA* **85**:9664-9668.

[2]Le Beau, M.M., Westbrook, C.A., Diaz, M.O., Rowley, J.D., and Oren, M. (1985) Translocation of the p53 gene in t(15;17) in acute promyelocytic leukemia. *Nature* **316**:826-828.

[3]Drabkin, H.A., Bradley, C., Hart, I., Bleskan, J., Li, F.P., and Patterson, D. (1985) translocation of c-*myc* in the hereditary renal cell carcinoma associated with t(3;8)(p14.2;q24.13) chromosomal translocation. *PNAS USA* **81**:6980-6984.

judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 48-50 of Application No. 08/487,387.

VII. Grouping of Claims

1. For the purposes of the rejection of claims 1, 48, and 50-58 under 35 U.S.C. § 103(a) as purportedly obvious over U.S. Patent 4,710,465 to Weissman et al in view of Lichter et al (1988) and Le Beau et al (1985) and Drabkin et al (1985), it is the Applicants' intention that those claims stand or fall together.

2. For the purposes of the provisional rejection of claims 1, 48, and 50-58 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 48-50 of Application No. 08/487,387, it is the Applicants' intention that the claims stand or fall together.

VIII. Argument

1. *The Rejection of Claims 1, 48, and 50-58 under 35 U.S.C. § 103(a) as purportedly obvious over U.S. Patent 4,710,465 to Weissman et al. in view of Lichter et al. (1988) and Le Beau et al. (1985) and Drabkin et al. (1985).*

The alleged teachings of Weissman et al were recently set forth in the Official Action mailed August 15, 2000 (Paper No. 26). On page 4 of the Official Action, the Examiner stated:

> Weissman et al. as summarized of record discloses the preparation of large unique sequence probes sets for hybridization assay of various chromosomal abberations including translocations. Motivation for assaying translocations is given in column 2, lines 13-39. The study of gene organization, of which translocations are clearly one type, are the subject of the Weissman et al. invention as noted in column 5, lines 53-58. Weissman et al., however, does not disclose interphase target assays nor specifically assaying directed to translocations in chromosomes 3 and/or 17.

The alleged teachings of Lichter et al., Le Beau et al. and Drabkin et al. were set forth on page 5 of the Official Action, mailed August 15, 2000 (Paper No. 26):

> Lichter et al. disclose interphase target assays for genetic abnormalities

utilized in an hybridization assay format. Several chromosomal regions which are distinctly detectable in such interphase samples are described in the paragraph bridging the first and second columns on page 9664. This description and the results in Lichter et al. give a reasonable expectation of success for such interphase assays, also as being equivalently usable as metaphase target based assays.

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Le Beau et al. in the abstract discloses chromosome 17 translocations as motivated targets regarding acute promyelocytic leukemia. This is motivation to assay for such translocation events.

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Drabkin et al. in the abstract discloses a translocation involving chromosome 3 as being reported in a family with renal cell carcinoma. Other familial chromosome 3 translocations in the paracentromeric region is described in the paragraph bridging the first and second columns on page 6980. This is motivation to assay for such translocation events.

In response, Applicants maintain that the present invention is not obvious over the cited publications. At the very least, the rejection is improper for several reasons. Weissman fails to disclose or even suggest the claimed invention directed to staining targeted chromosomal material based upon a nucleic acid segment employing unique sequence high complexity nucleic acid probes of greater than 50,000 bases, wherein said targeted chromosomal material is a genetic rearrangement associated with chromosome 3 and/or chromosome 17 in humans. Nor does Weissman provide motivation to detect chromosomal rearrangements using unique sequence probes. Weissman instead seeks to "determine the distance between, and/or orientation of two known genomic gene regions which are separated by a gene spacing of between 20 and 2,000 kilobases" (col. 6, lines 55-59). Further, Weissman discloses only mapping to *metaphase* spreads (see, for example, Figure 5, Section VI and Example XI), not a method of staining targeted *interphase* chromosomal material. There is no suggestion in this publication that interphase chromosomal material could be reliably stained as claimed in the present invention. The Examiner accepts this assertion in an Advisory Action mailed on January 8, 1998 (Paper No. 12) on page 3, acknowledging that "Weissman et al. does not contain disclosure of interphase chromosomal target material."

However, the Examiner asserts that these deficiencies are overcome with the

Lichter, Le Beau and Drabnik publications. Specifically, in the Office Action mailed on August 15, 2000 (Paper No. 26), the Examiner states:

> ...it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the instant invention because Weissman et al. generically suggests and motivates chromosomal abnormality hybridization assays with large unique probe sets. Lichter et al. describes hybridization assays utilizing interphase targets. Hybridization assays are generally utilized by Weissman et al. for the invention therein disclosed. Le Beau et al. and Drabkin et al. describe and motivate assay of chromosomes 17 and 3, respectively, as a target for hybridization assay due to translocations involving this chromosome. These disclosures together motivate and thus describe the instant invention.

This argument is flawed *at the very least* because the Lichter et al. publication is not prior art. This application claims priority of U.S. Application Serial No. 06/819,314, filed January 16, 1986, and U.S. Application Serial No. 06/937,793, filed December 4, 1986. Both of these applications were filed before the publication of the Lichter et al. article in December 1988. Accordingly, the Lichter et al. article is not properly cited as prior art against the present application. The Examiner has conceded that the present claims are not *prima facie* obvious over the Weissman patent alone and neither Le Beau et al. nor Drabkin et al. teach staining of interphase material. Thus, the Applicants strongly maintain that a *prima facie* case of obviousness has not been made out.

The Examiner has argued that the present claims are not supported by the noted 1986 priority applications. Specifically, on page 3 of the Office Action mailed March 17, 1999 (Paper No. 18), the Examiner states:

> Applicants further argue that priority to earlier parents should be given based on generic chromosomal detection disclosure in the parents. Such generic chromosomal detection lacks the specific citation of chromosomes 3 and 17 and particular functional embodiments and therefore priority is deemed to be lacking in the parents.

In response, Applicants maintain that support for the claims to the present invention may be found at the very least in U.S. Application Serial No. 06/819,314, filed January 16, 1986, at pages 11-14 and pages 31-38 and in U.S. Application Serial No. 06/937,793, filed December 4, 1986, at pages 8-15 and pages 32-39. Specifically, support for the recitation

that the genetic rearrangement may be associated with chromosome 3 and/or chromosome 17 is the description that the staining reagents useful in the invention are specific to single chromosomes at page 10, lines 17-21 of U.S. Application Serial No. 06/819,314, and at page 11, lines 1-5 of U.S. Application Serial No. 06/937,793. It was well-known, long before the present application was filed, that there is a low, finite number (24) of different chromosomes possible in human cells. Nevertheless, the Examiner argues that the rejected claims do not find written description support in the instant application because Applicants did not specifically name chromosomes 3 and 17. Applicants respectfully submit that the Examiner's position is untenable. This can be seen from the fact that merely listing chromosomes 1-22, X, and Y individually, and stating that translocations between any of the listed chromosomes could be detected, would remove the basis for this rejection. The Examiner's denial of benefit of Applicants' 1986 priority applications elevates form over substance to an extreme degree.

In examining whether a claim satisfies the written description requirement of 35 U.S.C. § 112, first paragraph, it must be determined whether the specification conveys, "with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she [i.e., the inventor] was in possession of the invention, i.e., whatever is now claimed." *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). It strains credibility to argue that one of ordinary skill would not have understood Applicants' 1986 priority applications to encompass detection of translocations between particular chromosomes, simply because the specification does not list each of the 24 possible chromosomes. Applicants strenuously maintain that one skilled in the art would reasonably believe the generic description of staining targeted chromosomal material to detect genetic rearrangements to not be limiting and to describe each of the chromosomes, *including chromosomes 3 and 17*, as being the targeted material.

In view of the fact that support may be found in the instant application, which is identical to the series of applications from which priority is claimed as a divisional and continuation, and support may be found in the 06/819,314 and 06/937,793 applications filed in 1986 from which priority is claimed as a continuation-in-part, Lichter et al.

For the foregoing reasons, it is submitted that the Examiner's rejections of claims 1, 48, and 50-58 were erroneous, and reversal of his decisions is respectfully requested.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: _____
Malcolm K. McGowan, Ph.D.
Registration No. 39,300

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Date: March 13, 2001

APPENDIX A

The Appealed Claims

1. (Four times Amended) A method of staining targeted interphase chromosomal material based upon a nucleic acid segment employing a unique sequence high complexity nucleic acid probe of greater than about 50,000 bases, wherein said targeted chromosomal material is a genetic rearrangement associated with chromosome 3 and/or chromosome 17 in humans, said method comprising employing said chromosomal material and a unique sequence high complexity nucleic acid probe of greater than about 50,000 bases in *in situ* hybridization, wherein the chromosomal material is present in a morphologically identifiable cell nucleus; allowing said probe to bind to said targeted chromosomal material; and detecting said bound probe, wherein bound probe is indicative of the presence of target chromosomal material.

48. (Twice Amended) A method of staining targeted interphase chromosomal material based upon a nucleic acid segment employing a unique sequence high complexity nucleic acid probe of greater than about 40 kb, wherein said targeted chromosomal material is a genetic rearrangement associated with chromosome 3 and/or chromosome 17 in humans, said method comprising contacting said chromosomal material with a unique sequence high complexity nucleic acid probe of greater than about 40 kb, wherein the chromosomal material is present in a morphologically identifiable cell nucleus; allowing said probe to bind to said targeted chromosomal material; and detecting said bound probe, wherein bound probe is indicative of the presence of target chromosomal material.

50. (Twice Amended) A method of staining targeted interphase chromosomal material based upon a nucleic acid segment employing a unique sequence high complexity nucleic acid probe of greater than about 50,000 bases, wherein said targeted interphase chromosomal material is a genetic rearrangement associated with chromosome 3 and/or chromosome 17 in humans, said method comprising contacting said interphase chromosomal material with a unique sequence high complexity nucleic acid probe of greater than about 50,000 bases, wherein the chromosomal material is present in a morphologically identifiable cell nucleus; allowing said probe to bind to said targeted interphase chromosomal material; and detecting said bound probe, wherein bound probe is indicative of the presence of target interphase chromosomal material.

51. The method of claim 48, wherein the genetic rearrangement is a translocation or an inversion.

52. The method of claim 48, wherein the unique sequence high complexity probe is labeled.

53. The method of claim 52, wherein the labeled unique sequence high complexity nucleic acid probe comprises fragments complementary to a single chromosome, fragments complementary to a subregion of a single chromosome, fragments complementary to a genome or fragments complementary to a subregion of a genome.

54. The method of claim 48, wherein the interphase chromosomal material is interphase chromosomal DNA.

55. The method of claim 50, wherein genetic rearrangement is a translocation or an inversion.

56. The method of claim 50, wherein the unique sequence high complexity nucleic acid probe is labeled.

57. The method of claim 56, wherein said labeled unique sequence high complexity nucleic acid probe comprises fragments complementary to a single chromosome, fragments complementary to a subregion of a single chromosome, fragments complementary to a genome or fragments complementary to a subregion of a genome.

58. The method of claim 50, wherein the interphase chromosomal material is interphase chromosomal DNA.

APPENDIX B

Cited Art

Lichter, P., Cremer, T., Tang, C., Watkins, P.C., Manuelidis, L., and Ward, D.C. (1988) Rapid detection of human chromosome 21 aberrations by *in situ* hybridization. *PNAS USA* **85**:9664-9668.

Le Beau, M.M., Westbrook, C.A., Diaz, M.O., Rowley, J.D. and Oren, M. (1985) Translocation of the p53 gene in t(15;17) in acute promyelocytic leukemia. *Nature* **316**:826-828.

Drabkin, H.A., Bradley, C., Hart, I., Bleskan, J., Li, F.P. and Patterson, D. (1985) translocation of c-*myc* in the hereditary renal cell carcinoma associated with t(3;8)(p14.2;q24.13) chromosomal translocation. *PNAS USA* **81**:6980-6984.

U.S. Patent 4,710,465 (Weissman et al)

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